



## HSPB1 gene

heat shock protein family B (small) member 1

### Normal Function

The *HSPB1* gene provides instructions for making a protein called heat shock protein beta-1 (also called heat shock protein 27). This protein is a member of the heat shock protein family, which helps protect cells under adverse conditions such as infection, inflammation, exposure to toxins, elevated temperature, injury, and disease. Heat shock proteins block signals that lead to programmed cell death. In addition, they appear to be involved in activities such as cell movement (motility), stabilizing the cell's structural framework (the cytoskeleton), folding and stabilizing newly produced proteins, and repairing damaged proteins. Heat shock proteins also appear to play a role in the tensing of muscle fibers (muscle contraction).

Heat shock protein beta-1 is found in cells throughout the body and is particularly abundant in nerve and muscle cells. In nerve cells, this protein helps to organize a network of molecular threads called neurofilaments that maintain the diameter of specialized extensions called axons. Maintaining proper axon diameter is essential for the efficient transmission of nerve impulses. Although it is thought to play a role in muscle contraction, the specific function of heat shock protein beta-1 in muscle cells is unclear.

### Health Conditions Related to Genetic Changes

#### Charcot-Marie-Tooth disease

At least three *HSPB1* gene mutations have been reported in individuals with a form of Charcot-Marie-Tooth disease known as type 2F. Charcot-Marie-Tooth disease is a group of progressive disorders that affect the peripheral nerves. Peripheral nerves connect the brain and spinal cord to muscles and to sensory cells that detect sensations such as touch, pain, heat, and sound.

Each *HSPB1* gene mutation that causes Charcot-Marie-Tooth disease changes a single protein building block (amino acid) used to make heat shock protein beta-1. One mutation replaces the amino acid serine with the amino acid phenylalanine at protein position 135 (written as Ser135Phe or S135F). Other mutations replace the amino acid arginine with the amino acid tryptophan at position 127 (Arg127Trp or R127W) or position 136 (Arg136Trp or R136W). These mutations alter a region of the protein that is critical for heat shock protein beta-1 to function properly.

It is unclear how *HSPB1* gene mutations lead to the axon abnormalities that are characteristic of type 2F Charcot-Marie-Tooth disease. Researchers suggest that

molecules of altered heat shock protein beta-1 cluster together (aggregate) and interfere with the normal functions of nerve cells, particularly axon function. Another possibility is that the altered protein disrupts the assembly of neurofilaments, which affects axon diameter and impairs the transmission of nerve impulses.

### distal hereditary motor neuropathy, type II

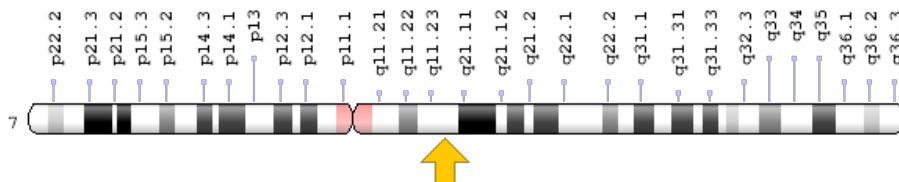
Researchers have identified at least six *HSPB1* gene mutations that cause a condition called distal hereditary motor neuropathy, type II, which is similar to Charcot-Marie-Tooth disease. Distal hereditary motor neuropathy, type II affects peripheral nerves and is characterized by progressive weakness, primarily in the feet and legs. Unlike Charcot-Marie-Tooth disease, distal hereditary motor neuropathy, type II does not affect sensory cells.

*HSPB1* gene mutations that cause distal hereditary motor neuropathy, type II change single amino acids in heat shock protein beta-1. It is not well understood how these mutations lead to the signs and symptoms of this disorder. As with the *HSPB1* gene mutations that cause Charcot-Marie-Tooth disease, studies suggest that the altered protein may be more likely to form aggregates and block the transport of substances that are essential for the proper function of nerve axons. The disruption of other cell functions in which this protein is involved may also contribute to peripheral nerve disease.

### Chromosomal Location

Cytogenetic Location: 7q11.23, which is the long (q) arm of chromosome 7 at position 11.23

Molecular Location: base pairs 76,302,558 to 76,304,297 on chromosome 7 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

### Other Names for This Gene

- CMT2F
- heat shock 27kDa protein 1
- heat shock protein beta-1

- HS.76067
- Hsp25
- HSP27
- HSP28
- HSPB1\_HUMAN
- SRP27
- stress-responsive protein 27

## **Additional Information & Resources**

### GeneReviews

- Charcot-Marie-Tooth Neuropathy Type 2  
<https://www.ncbi.nlm.nih.gov/books/NBK1285>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28HSPB1%5BTIAB%5D%29+OR+%28HSP27%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D>

### OMIM

- HEAT-SHOCK 27-KD PROTEIN 1  
<http://omim.org/entry/602195>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
<http://atlasgeneticsoncology.org/Genes/HSPB1ID40880ch7q11.html>
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=HSPB1%5Bgene%5D>
- HGNC Gene Family: Small heat shock proteins  
<http://www.genenames.org/cgi-bin/genefamilies/set/585>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=5246](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=5246)
- Inherited Peripheral Neuropathies Mutation Database  
<http://www.molgen.ua.ac.be/CMTMutations/Mutations/Mutations.cfm?Context=36>

- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/3315>
- UniProt  
<http://www.uniprot.org/uniprot/P04792>

## Sources for This Summary

- Ackerley S, James PA, Kalli A, French S, Davies KE, Talbot K. A mutation in the small heat-shock protein HSPB1 leading to distal hereditary motor neuronopathy disrupts neurofilament assembly and the axonal transport of specific cellular cargoes. *Hum Mol Genet.* 2006 Jan 15;15(2):347-54. Epub 2005 Dec 20.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16368711>
- Benndorf R, Welsh MJ. Shocking degeneration. *Nat Genet.* 2004 Jun;36(6):547-8.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/15167925>
- Dierick I, Baets J, Irobi J, Jacobs A, De Vriendt E, Deconinck T, Merlini L, Van den Bergh P, Rasic VM, Robberecht W, Fischer D, Morales RJ, Mitrovic Z, Seeman P, Mazanec R, Kochanski A, Jordanova A, Auer-Grumbach M, Helderma-van den Enden AT, Wokke JH, Nelis E, De Jonghe P, Timmerman V. Relative contribution of mutations in genes for autosomal dominant distal hereditary motor neuropathies: a genotype-phenotype correlation study. *Brain.* 2008 May;131(Pt 5):1217-27. doi: 10.1093/brain/awn029. Epub 2008 Mar 5.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18325928>
- Dierick I, Irobi J, De Jonghe P, Timmerman V. Small heat shock proteins in inherited peripheral neuropathies. *Ann Med.* 2005;37(6):413-22. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16203614>
- Evgrafov OV, Mersiyanova I, Irobi J, Van Den Bosch L, Dierick I, Leung CL, Schagina O, Verpoorten N, Van Impe K, Fedotov V, Dadali E, Auer-Grumbach M, Windpassinger C, Wagner K, Mitrovic Z, Hilton-Jones D, Talbot K, Martin JJ, Vasserman N, Tverskaya S, Polyakov A, Liem RK, Gettemans J, Robberecht W, De Jonghe P, Timmerman V. Mutant small heat-shock protein 27 causes axonal Charcot-Marie-Tooth disease and distal hereditary motor neuropathy. *Nat Genet.* 2004 Jun;36(6):602-6. Epub 2004 May 2.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/15122254>
- Fontaine JM, Rest JS, Welsh MJ, Benndorf R. The sperm outer dense fiber protein is the 10th member of the superfamily of mammalian small stress proteins. *Cell Stress Chaperones.* 2003 Spring;8(1):62-9.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12820655>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC514854/>
- GeneReview: Charcot-Marie-Tooth Neuropathy Type 2  
<https://www.ncbi.nlm.nih.gov/books/NBK1285>
- OMIM: HEAT-SHOCK 27-KD PROTEIN 1  
<http://omim.org/entry/602195>
- Houlden H, Laura M, Wavrant-De Vrièze F, Blake J, Wood N, Reilly MM. Mutations in the HSP27 (HSPB1) gene cause dominant, recessive, and sporadic distal HMN/CMT type 2. *Neurology.* 2008 Nov 18;71(21):1660-8. doi: 10.1212/01.wnl.0000319696.14225.67. Epub 2008 Oct 1.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18832141>

- Ikeda Y, Abe A, Ishida C, Takahashi K, Hayasaka K, Yamada M. A clinical phenotype of distal hereditary motor neuronopathy type II with a novel HSPB1 mutation. *J Neurol Sci.* 2009 Feb 15; 277(1-2):9-12. doi: 10.1016/j.jns.2008.09.031. Epub 2008 Oct 25.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18952241>
- James PA, Rankin J, Talbot K. Asymmetrical late onset motor neuropathy associated with a novel mutation in the small heat shock protein HSPB1 (HSP27). *J Neurol Neurosurg Psychiatry.* 2008 Apr;79(4):461-3. doi: 10.1136/jnnp.2007.125179.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18344398>
- Kijima K, Numakura C, Goto T, Takahashi T, Otagiri T, Umetsu K, Hayasaka K. Small heat shock protein 27 mutation in a Japanese patient with distal hereditary motor neuropathy. *J Hum Genet.* 2005;50(9):473-6. Epub 2005 Sep 10.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16155736>
- Niemann A, Berger P, Suter U. Pathomechanisms of mutant proteins in Charcot-Marie-Tooth disease. *Neuromolecular Med.* 2006;8(1-2):217-42. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16775378>
- Tang B, Liu X, Zhao G, Luo W, Xia K, Pan Q, Cai F, Hu Z, Zhang C, Chen B, Zhang F, Shen L, Zhang R, Jiang H. Mutation analysis of the small heat shock protein 27 gene in chinese patients with Charcot-Marie-Tooth disease. *Arch Neurol.* 2005 Aug;62(8):1201-7.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16087758>
- Zhai J, Lin H, Julien JP, Schlaepfer WW. Disruption of neurofilament network with aggregation of light neurofilament protein: a common pathway leading to motor neuron degeneration due to Charcot-Marie-Tooth disease-linked mutations in NFL and HSPB1. *Hum Mol Genet.* 2007 Dec 15; 16(24):3103-16. Epub 2007 Sep 19.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17881652>
- Züchner S, Vance JM. Molecular genetics of autosomal-dominant axonal Charcot-Marie-Tooth disease. *Neuromolecular Med.* 2006;8(1-2):63-74. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16775367>

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